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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,925	04/02/2004	Klaus Bosslet	DEAV1993/B005 US CNT 2	9424

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EXAMINER	
NATARAJAN, MEERA	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
01/21/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/815,925	BOSSLET ET AL.	
	Examiner	Art Unit	
	MEERA NATARAJAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9,16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/22/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's claim amendments in the reply filed on 9/22/2010 is acknowledged and entered into the record.

2. Accordingly, Claims 1, 9, 16 and 17 are pending and will be examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 9, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 1 recites the limitation "said bifunctional fusion glycoprotein". There is insufficient antecedent basis for this limitation in the claim. Appropriate correction is required.

6. Claim 9 recites the limitation "the tumor cell marker" in line 1 and "the second portions" in line 2. There is insufficient antecedent basis for these limitations in the claim. Appropriate correction is required.

7. Claim 1 seems to be directed to an antibody which binds to the specific carbohydrates listed in Claim 1, rather than "an epitope of a tumor specific antigen", as was previously claimed. It is believed, this deletion in Claim 1 was inadvertent and appropriate correction is required.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 9, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Seeman et al. (EP-A-0 501 215, IDS).

10. The claims are currently directed to a pharmaceutical composition comprising a compound comprising a carbohydrate complement, a humanized two-chain fusion protein composed of a humanized VH-CH1-hinge-S-human β-glucuronidase chain and of a humanized VLCL chain which binds specifically to galactose, mannose, N-acetylgucosamine, fucose and N-acetylneuraminic acid, wherein said bifunctional fusion glycoprotein has been synthesized in CHO cells and wherein the amount of the carbohydrates given as mol monosaccharide/mol fusion protein is 1.40 of galactose, 7.04 of mannose, 4.35 of N-acetyl glucosamine, 0.6 of fucose and 0.54 of N-acetylneuraminic acid, the cells having been selected for a high level of expression of the glycoprotein, and wherein S is a polypeptide spacer.

11. Seeman et al. disclose a humanized, two-chain fusion protein which is composed of two polypeptide chains prepared by genetic manipulation. One chain was prepared by linking the nucleotide sequences that encode a humanized V_HC_H hinge S region to the nucleotide sequence which encodes a human B-glucuronidase (S=oligonucleotide

encoding a polypeptide spacer). Seeman et al. further discloses following transfection and expression in suitable expression systems, preferably BHK or CHO cells, the nucleotide sequence which encodes the humanized V_LC_L chain together with the above-mentioned nucleotide sequence, produces the humanized two-chain fusion protein (teachings summarized in instant specification, p. 11). Seeman et al. disclose antibody binding fragments of anti-CEA monoclonal antibody (BW431/26) and a pharmaceutical composition comprising the fusion protein, wherein the fusion protein was dissolved in tris/HCl buffer.

12. Because Seeman et al. disclose expressing the fusion protein in the same cell line (CHO) as the instant claims and discloses using the same expression vector (pABstop), the specific amounts of carbohydrates disclosed in the instant claims would be inherently taught by Seeman et al., because the production of the fusion protein in the same cell line (CHO) using the same vector as the instant application would produce a protein comprising the same composition and amounts of carbohydrates.

13. The burden falls on the applicant to prove that the antibodies would be different because the office does not have the facilities and resources to provide the factual evidence needed to establish a difference between the carbohydrate makeup of the claimed antibody and that disclosed by Seeman et al. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. Claims 1, 9, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seeman et al. (EP-A-0 501 215) in view of Bosslet et al. (British Journal of Cancer 65; 234-238, 1992) and Jahde et al. (Cancer Research, Vol. 52:6209, 1992).

17. The claims are currently directed to a pharmaceutical composition comprising a compound comprising a carbohydrate complement, a humanized two-chain fusion protein composed of a humanized V_H-CH1-hinge-S-human β-glucuronidase chain and of a humanized V_LC_L chain which binds specifically to galactose, mannose, N-acetylglucosamine, fucose and N-acetylneuraminic acid, wherein said bifunctional fusion glycoprotein has been synthesized in CHO cells and wherein the amount of the

carbohydrates given as mol monosaccharide/mol fusion protein is 1.40 of galactose, 7.04 of mannose, 4.35 of N-acetyl glucosamine, 0.6 of fucose and 0.54 of N-acetylneuraminic acid, the cells having been selected for a high level of expression of the glycoprotein, and wherein S is a polypeptide spacer. The pharmaceutical composition additionally comprises an agent capable of lowering the pH in a tumor to be treated.

18. The teachings of Seeman et al. are presented in the 102(b) rejection set forth above. Seeman et al. does not teach an additional agent capable of lowering the pH in a tumor to be treated. This deficiency is made up for by Bosslet et al. and Jahde et al.

19. Bosslet et al. teach that the activity of B-glucuronidase increases at a pH that is lower than physiological pH (p. 236, 2nd col.)

20. Jahde teach methods of lowering intracellular pH of tumors comprising administering glucose (p. 62310, 2nd col. Results section).

21. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the references so as to modify the pharmaceutical composition as taught by Seeman et al. to include an agent that lowers the intracellular pH of a tumor in view of Bosslet and Jahde. One would have been motivated to do so because Bosslet teaches that the activity of B-glucuronidase increases at a pH that is lower than physiological pH and Jahde provides agents which are capable of reducing intracellular pH. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by modifying the pharmaceutical composition as taught by Seeman et al. to include an agent that lowers the intracellular

pH of tumor in view of Bosslet and Jahde, one would achieve a pharmaceutical composition having an agent which increases the enzymatic activity of B-glucuronidase.

Conclusion

22. Claims 1, 9, 16 and 17 are rejected.

23. No Claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is (571)270-3058. The examiner can normally be reached on Monday-Friday, 9:00AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MN/

/Misook Yu/
Supervisory Patent Examiner, Art Unit 1643